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(54) Title: AMINO-HETEROCYCLES AS VR-1 ANTAGONISTS FOR TREATING PAIN

$$(R^{1})_{n} - Ar_{1} - V \xrightarrow{V} R^{2}$$
(I)

(57) Abstract: the present invention provides a compound of formula (I): wherein V represents NR<sup>5</sup>, O, S, SO or S(O)<sub>2</sub>; W and X each independently represent CH or N; Y represents N, CH or C-Ar<sub>2</sub>, with the proviso that at least one, but no more than two, of W, X and Y are N; Z represents CH or C-Ar2, with the proviso that when Y is N or CH then Z is C-Ar2, and with the further proviso that when Y is C-Ar<sub>2</sub> then Z is CH; Ar<sub>1</sub> represents a fused 9 or 10 membered heterobicyclic ring system containing one, two, three or four heteroatoms selected from nitrogen, oxygen and sulfur, wherein at least one of the rings in said ring system is aromatic; Ar<sub>2</sub> represents an aromatic ring selected from phenyl, pyridyl, pyrimidinyl and pyridazinyl which is optionally fused and substituted; R1  $represents\ halogen,\ hydroxy,\ oxo,\ C_{1-6}alkyl,\ C_{2-6}alkenyl,\ C_{2-6}alkynyl,\ haloC_{1-6}alkyl,\ hydroxyC_{1-6}alkyl,\ C_{1-6}alkoxy,\ haloC_{1-6}alkoxy,\ haloC_{1-6}alkoxy,\$ hydroxyC<sub>1-6</sub>alkoxy, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkoxy, C<sub>3-5</sub>cycloalkylC<sub>1-4</sub>alkyl, cyano, nitro, SR<sup>6</sup>, SOR<sup>6</sup>, SOR<sup>6</sup>, COR<sup>6</sup>, NR<sup>3</sup>COR<sup>6</sup>, CONR<sup>3</sup>R<sup>4</sup>, NR<sup>3</sup>SO<sub>2</sub>R<sup>6</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup>, -(CH<sub>2</sub>)<sub>m</sub>carboxy, esterified -(CH<sub>2</sub>)<sub>m</sub>carboxy or -(CH<sub>2</sub>)<sub>m</sub>NR<sup>3</sup>R<sup>4</sup>; R<sup>2</sup> represents hydrogen, halogen, hydroxy, C<sub>1-6</sub>alkyl, haloC<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkoxy, haloC<sub>1-6</sub>alkoxy, unsubstituted phenyl or phenyl substituted with one or two groups selected from halogen, C<sub>1.6</sub>alkyl, haloC<sub>1.6</sub>alkyl, C<sub>3.7</sub>cycloalkyl, C<sub>1.6</sub>alkoxy or haloC<sub>1.6</sub>alkoxy; R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen, C1-6alkyl, C2-6alkynyl, C3-7cycloalkyl or fluoroC1-6alkyl; or R3 and R4 and the nitrogen atom to which they are attached together form a heteroaliphatic ring of 4 to 7 ring atoms, optionally substituted by one or two groups selected from hydroxy or C<sub>1-4</sub>alkoxy, which ring may optionally contain as one of the said ring atoms an oxygen or a sulfur atom, S(O), S(O)<sub>2</sub>, or NR<sup>5</sup>; R<sup>5</sup> represents hydrogen, C<sub>1-4</sub>alkyl, hydroxyC<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl; R<sup>6</sup> represents hydrogen, C<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, unsubstituted phenyl, or phenyl substituted with one or two groups selected from halogen, C<sub>1-6</sub>alkyl, haloC<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkoxy or haloC<sub>1-6</sub>alkoxy; m is either zero or an integer from 1 to 4; n is either zero or an integer from 1 to 3; or a pharmaceutically acceptable salt, N-oxide or a prodrug thereof; a pharmaceutical composition comprising it; its use in methods of treatment; use of it for the manufacture of a medicament for treating VR-1 related conditions such as those in which pain and/or inflammation predominate; and methods of treatment using it.

